

Case Report

End Stage Renal Disease Patient With Spontaneous Tendo-Achilles Rupture



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New Mansoura General Hospital
CKD MBD Day - 28/Oct/2014



Chronic Kidney Disease Mineral & Bone Disorder



**Think Outside
The Box**

Case Scenarios Snapshots

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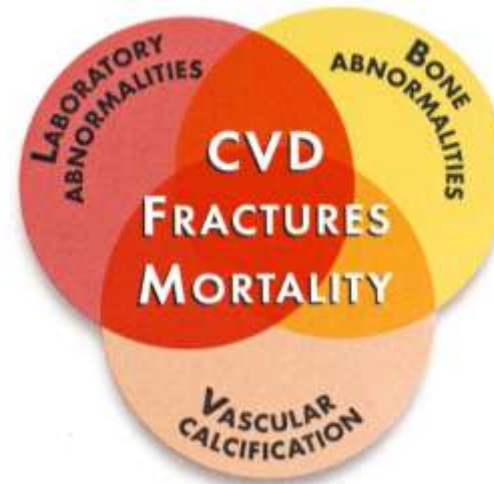
Case Report

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Table 1 | KDIGO classification of CKD-MBD and renal osteodystrophy

Definition of CKD-MBD

A systemic disorder of mineral and bone metabolism due to CKD manifested by either one or a combination of the following:

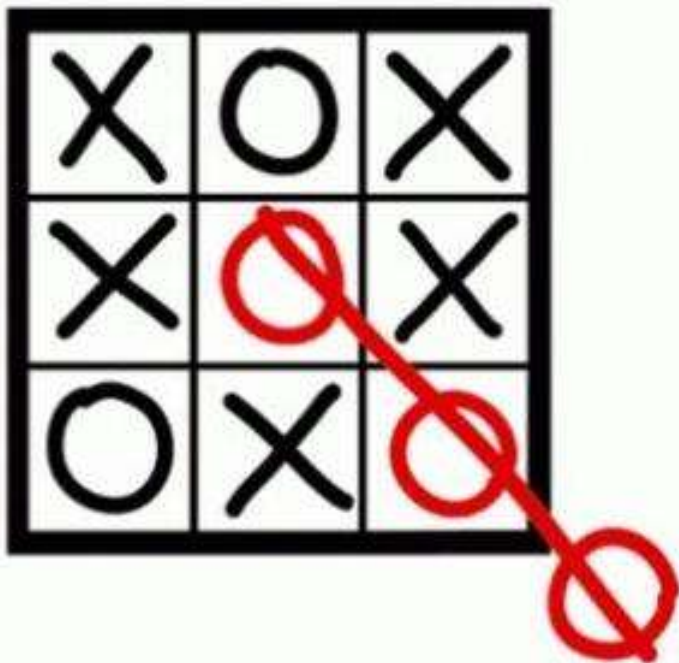
- Abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism.
- Abnormalities in bone turnover, mineralization, volume, linear growth, or strength.
- Vascular or other soft-tissue calcification.



CKD - MBD

CKD - MVD

CKD - MSD



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CKD patients may develop any intercurrent primary or secondary disorders rather than the expected course and complications of CKD





Thank You

Case 1

Case 1

40 years old female. ESRD and HTN following delivery in 2010. She is on maintenance haemodialysis.

Her main major complaint was bone pain all over her body.

- Ca: 11.2 mg/dl
- Phosphorous: 9 mg/dl
- PTH: 1900 pg/ml



- Cinacalcet 60 mg/d
- Ca carbonate
- Alphacalcidol
- Follow up after 2 weeks



- Ca: 11 mg/dl
- Phosphorous: 8 mg/dl
- PTH: 1750 pg/ml
- + Nausea

- Discussion regarding the probability of parathyroidectomy: the patient refused
- Cinacalcet 30 mg/d
- Ca carbonate
- Alphacalcidol
- Follow up after 4 weeks



Case 1

40 years old female. ESRD and HTN following delivery in 2010. She is on maintenance haemodialysis.

- **After 2 weeks (Cinacalcet):**

- ✓ PTH: 1200 pg/ml
- ✓ Ca: 9 mg/dl
- ✓ PO4: 5.5 mg/dl

But

- Persistent annoying nausea.

Gastrointestinal adverse events (mostly nausea and vomiting) are frequently associated with cinacalcet

European Medicines Agency: Mimpara: EPAR product information: Summary of product characteristics. Accessed April 30, 2015

- **What is the suspected cause of Nausea**

within accepted ranges.

- No evidence of infection or septicemia.
- No abdominal tenderness or rigidity.
- No change in bowel habits (constipation or diarrhea).

Cinacalcet GIT Adverse Effects

- Nausea (30% to 66%)
- Vomiting (26% to 52%)
- Diarrhea (21%)
- Anorexia (6% to 21%)
- Constipation (5% to 18%)
- Abdominal pain (11%)

Cinacalcet Induced N&V Mechanism

Cinacalcet stimulate the CaR present in:

- Hypothalamus & other brain regions controlling vomiting.
- Gastrointestinal tract.



Cinacalcet Induced N&V

How to avoid?

- Incidence of gastrointestinal adverse events is lower when Cinacalcet is administered:
 - ✓ with the first main meal after dialysis.
 - ✓ in the evening.

Schaefer RM et al. **The SENSOR Study**. Clin Nephrol 70: 126–134, 2008

**Bioavailability of Cinacalcet
increases by 50%–80% with food**

Martin KJ et al. Kidney Int 85: 191–197, 2014

Cinacalcet Induced N&V

How to avoid?

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 - ✓ with the first main meal after dialysis.
 - ✓ in the evening.

Schaefer RM et al. **The SENSOR Study**. Clin Nephrol 70: 126–134, 2008

- If symptoms do not abate:
 - ✓ reduction to the previous tolerated dose is often sufficient.

Jordi Bover et al. Clin J Am Soc Nephrol. Jul 29, 2015

Cinacalcet Induced N&V

How to avoid?

Measures for the control of cinacalcet-related nausea and vomiting	
Measure	
Tell the patient that cinacalcet is not an ulcer-inducing drug and explain the importance of the CKD-MBD treatment, including a potential beneficial cardiovascular effect	
Give cinacalcet with the main meal after dialysis	
Try cinacalcet in the evening	
Earlier use will allow lower doses	
Do not give up immediately if only mild/moderate symptoms are present	
Decrease or fractionate the dose if symptoms appear after a dose escalation	
Caution is advised with antiemetics, including metoclopramide (QT prolongation)	

Case 2

Case 2

50 years old male. ESRD secondary to chronic uncontrolled HTN. He is on maintenance haemodialysis.

- The patient medications:

- Cinalcet 60mg/d
- Ca acetate

- After 2 weeks:

- ✓ PTH: 1200 pg/ml
- ✓ Ca: 8.5 mg/dl
- ✓ PO4: 5.5 mg/dl



But

- A syncopal attack was witnessed during clinic examination.

- Severe Nausea.

- After 2 days:

- Patient presented by 3 syncopal attacks (especially with exercise).

- **Domperidone** was prescribed as a prokinetic
- Cinalcet was administered with meals



Case 2

50 years old male. ESRD secondary to chronic uncontrolled HTN. He is on maintenance haemodialysis.



What predisposes long QT syndrome in this patient?

Case 2

50 years old male. ESRD secondary to chronic uncontrolled HTN. He is on maintenance haemodialysis.

- Serum Ca: 6.8mg/dl (the patient omitted his Calcium carbonate supplement, which aggravates the hypocalcemic effect of Cinacalcet).
- The physician prescribed Domperidone for nausea symptomatic management.



What predisposes long QT syndrome in this patient?

Risk of Long QT with Cinacalcet Use

Hypocalcemia

- Cinacalcet is not on the list of all drugs that can affect QT interval.
- BUT hypocalcemia that may be associated with Cinacalcet use can prolong the QT interval.
- QT evaluation is not mandatory, BUT QT evaluation is advised in high-risk patients:
 - ✓ Familial history
 - ✓ Bradycardia
 - ✓ Recent cardiac ablation
 - ✓ Hypokalemia / Hypomagnesemia

Risk of Long QT with Cinacalcet Use

Hypocalcemia

- Cinacalcet should not be initiated if the calcium is <8.4 mg/dL.
- The dose should be increased based on monthly or quarterly PTH results, provided the corrected calcium is >7.8 mg/dL.

Risk of Long QT with Cinacalcet Use

Anti-emetic / Prokinetic

Nausea & Vomiting are very common with the use of Cinacalcet

Take care

Antiemetic drugs (mainly metoclopramide)
Gastroprokinetic drugs (domperidone, cisapride, or ondansetron)

affect the electrocardiographic QT interval

Case 3

Case 3

55 years old male. DM, HTN, CHF, ESRD and he is on maintenance HD.

- The patient medications:

- ESA (Hb: 8.5 g/dl)
- Alphaclacidol
- Ca carbonate
- Carvidolol
- Lisinopril
- Digoxin (modified to renal impairment)
- DM is well controlled on insulin therapy



- Before the start of the traditional HD session, the patient complaints of:

- Drowsiness
- Headache
- Anorexia
- Diarrhea
- Palpitation

- After 30 min of HD session:

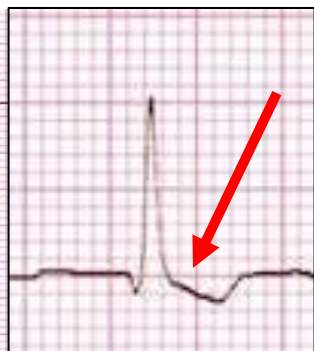
- Patient C/O of exacerbation of palpitation.
- BP: 80/50 mmHg
- Loss of consiusness

- Symptoms were attributed to anemia and uremia.

- Resuscitation was done.
- ECG & Lab Ix were done.

Case 3

55 years old male. DM, HTN, CHF, ESRD and he is on maintenance HD.



Reverse tick sign



Digitalis effect



Salvador Dali's mustache (saddle shape)



What predisposes digoxin toxicity in this patient?

Case 3

55 years old male. DM, HTN, CHF, ESRD and he is on maintenance HD.

- Serum Ca: 13.5mg/dl (the patient said that he increased the dose of Alphacalcidol and Ca carbonate by his own because he felt bony pains).

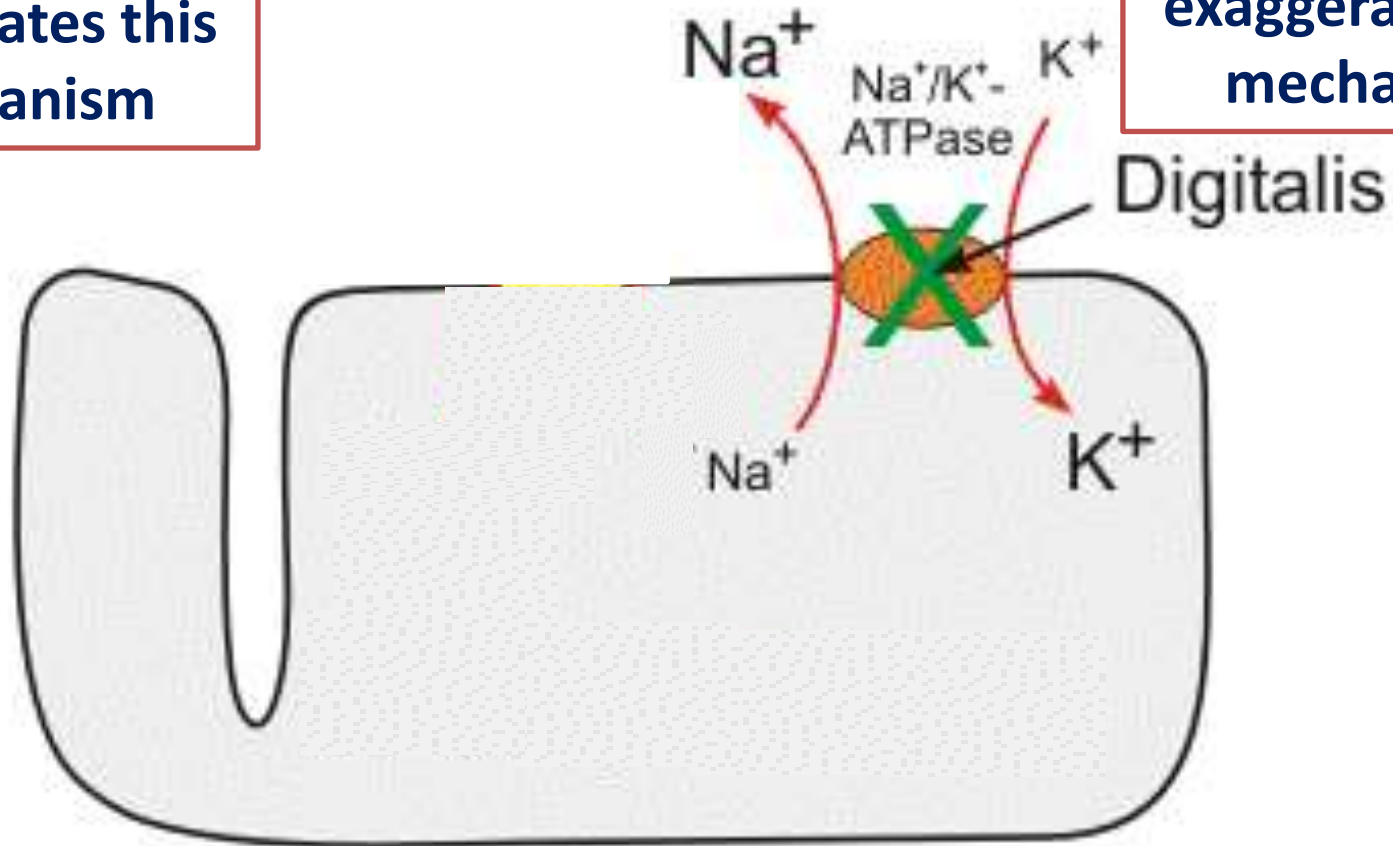


What predisposes digoxin toxicity in this patient?

Digoxin – Calcium/Potassium

Hypercalcemia
exaggerates this
mechanism

Hypokalemia
exaggerates this
mechanism



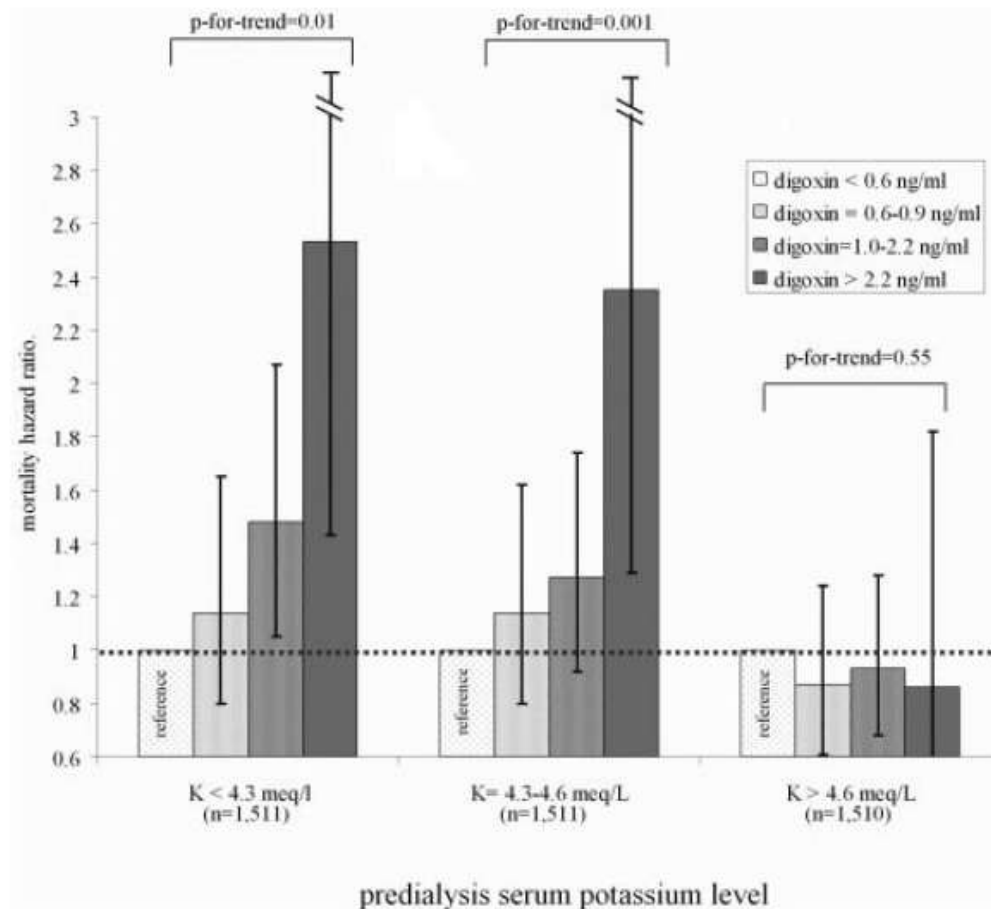
Digitalis and Hemodialysis Is a Bad Combination

David R. Thiemann

- Narrow therapeutic window
- Long half-life
- Potential for lethal arrhythmias (especially in the context of HD-induced hypokalemia)

Digoxin Associates with Mortality in ESRD

Kevin E. Chan,^{*†} J. Michael Lazarus,^{*} and Raymond M. Hakim^{*}



Case 4

Case 4

52 years old female. HTN, Hypothyroidism, ESRD on maintenance HD.

The patient medications:

- ESA
- Ca carbonate
- Felodipine
- L-Thyroxine 75 mcg/d
(Last tx 2 months ago:
 $TSH \leq 2$ mIU/L, $FT_4 = 1.5$ ng/dL)



The patient started to complaint of:

- Drowsiness
- Headache
- Anorexia
- Constipation
- Somnolence

- L-Thyroxine dose increased to 150 mcg/d



- $TSH = 9.8$ mIU/L mIU/L
- $FT_4 = 0.2$ ng/dL



What is the cause of ineffective L-thyroxine therapy?

- Persisting Lab criteria of hypothyroidism

100 mcg/d

Case 4

52 years old female. HTN, Hypothyroidism, ESRD on maintenance HD.

- The patient was taking Ca carbonate & L-Thyroxine pills at the same time

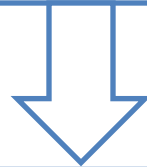


What is the cause of ineffective L-thyroxine therapy?

L-Thyroxine & Ca Carbonate

L-Thyroxine adsorbs to calcium carbonate in an acidic environment, which may reduce its bioavailability

P V Eligar. The West London Medical Journal. Vol 3 No 4 pp 9 -14, 2011



Separate the doses of the thyroid product and the oral calcium supplement by at least 4 hours.

 Lexi-comp® 2015

Case 5

Case 5

45 years old male. HTN, ESRD on maintenance HD.

You prescribed Calcimate[®]
(Ca Carbonate)

Case 5

45 years old male. HTN, ESRD on maintenance HD.

The patient got the drug pamphlet for you



Calcimate

500 mg CAPSULES

Calcium Carbonate

Composition :

Each capsule contains Calcium Carbonate 500 mg .

Properties :

Pharmacology :

Calcimate is considered as a dietary supplement where calcium intake is inadequate. Calcium is very important for bones and teeth, specially for elderly to reduce bone fractures and risk of osteoporosis.

Indications & Usage :

- * Calcimate capsule are used as a calcium supplement in hypocalcemia states e.g. pregnancy, lactation
- * Calcimate capsule are used as supplement to reduce the risk of osteoporosis
- * In elderly specially women which tend to have fragile bone in later ages
- * Used as supplement during teenagers and early adults to build and maintain good bone health

Contra – Indications :

- Renal impairment .
- Hypersensitivity and hypercalciuria.
- Gastric and duodenal ulcers.

Side – Effects :

- Sometimes constipation may occur with high calcium carbonate intake.
- Hypercalcemia.
- Mild gastrointestinal disturbance .
- arrhythmias

Drug – Interactions :

- Calcium salts may enhance the cardiac effects of digitalis glycosides.
- Calcium carbonate may interfere with the absorption of other drugs given concomitantly, e.g. tetracyclines and bisphosphonates
- Diuretics : Increased risk of hypercalcemia with thiazides

Warnings & Precautions :

- Administration of high doses of vitamin D should be avoided during calcium therapy unless it is prescribed.

Dosage & Administration :

- One capsule daily with meals or according to physician instructions.
- This dietary requirement varies with age and is relatively greater in pregnancy and lactation , adequate calcium intake is important but daily intake above 2000 mg calcium are not likely to provide any additional benefit .

Packing :

- Box containing 1002 capsules each in 167strips each of 6 capsules
- Box containing 600 capsules each in 100 strips each of 6 capsules
- Box containing 120 capsules each in 20 strips each of 6 capsules
- Box containing 12 capsules each in 2 strips each of 6 capsules

Storage :

- Store in a temperature not exceeding 25 °C.
- Keep in dry place, protect from light.
- Keep out of reach of children

Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sales the medicament.
The doctor and the pharmacist are experts in medicine. It's benefits and risks.
Do not by yourself interrupt the period of treatment prescribed for you.
Do not repeat the same prescription without consulting your doctor.
Keep medicament out of children reach

Council of Arab Health Ministers and Union of Arab Pharmacists

CKD – MBD

Drug Related Issues

Case Scenarios

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